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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
PHAM, AUDREY S	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 03/30/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/626,905	FRANZOSO ET AL.	
	Examiner	Art Unit	
	Audrey S. Pham	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 January 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-35* is/are pending in the application.

4a) Of the above claim(s) *3-5 and 7-35* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2 and 6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☒ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Examiner's Response to Election/Restriction

The Election filed on January 06, 2006, in response to the Office Action Requirement for Restriction dated October 06, 2005 is acknowledged and has been entered. Applicant elected Group II, Claims 1-2, 6, 8 without traverse. Claims 3-5, 7, 9-35 have been withdrawn from further consideration by the examiner under 37 CFR 1. 142(b) as being drawn to non-elected inventions. In the Claim Amendment submitted on January 06, 2006, Applicant lists Claim 8 as withdrawn. Claims 1-2, 6, 8 are currently under consideration.

The amendment of Claim 6 to recite "...a cell-permeable peptide that competes with the Gad45β protein for the binding site of JNKK2" has been acknowledged and entered on the record.

Upon review and reconsideration, an election is required to determine a starting point for the examination of the claims. The requirement is set forth below:

Species Election

Claim 1 is generic to a plurality of patentably distinct species disclosed in the specification comprising the following targets: JNK1, JNK2, JNK3, MAPKKK (Mitogen Activated Protein Kinase Kinase Kinase): GCK, GCKR, ASK1/MAPKKK5, ASK2/MAPKKK6, DLK/MUK/ZPK, LZK, MEKK1, MEKK2, MEKK3, MEKK4/MTK1, MLK1, MLK2/MST, MLK3/SPRK/PTK1, TAK1, Tpl-2/Cot. MAPKK (Mitogen Activated Protein Kinase Kinase), MKK4/SEK1/SERK1/SKK1/JNKK1, MKK7/SEK2/SKK4/JNKK2. MAPK (Mitogen Activated Kinase), JNK1/SAPKγ/SAPK1c, JNK2/SAPKα/SAPK1a, JNK3/SAPKβ/SAPK1b/p49F12 (page 60, paragraph 165), Gadd45 protein, and peptide mimetic that mimics the functions of Gadd45 protein.

The products of the above species represent separate and distinct targets with different structures and functions such that one species could not be interchanged with the other. As such, each species would require different searches and the consideration of different patentability issues.

Applicant is required under 35 U.S.C. 121 to elect a single disclosed species for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Applicant's Election to the New Restriction Requirement

A telephone call was made on February 22, 2006 to request an election of species as set forth above. On February 23, 2006, Ms. Martin elected Gadd45 as the target. Ms. Martin affirmed that Claim 8, which is shown as withdrawn in the claims Amendment submitted on January 06. 2006, is in fact, withdrawn. Thus, claims 1, 2 and 6, as specifically drawn to Gadd45 proteins, are currently under prosecution and will be considered.

Affirmation of this telephone election, in writing, is required in response to this Office Action.

Specification Objections

The disclosure is objected to because the specification refers to peptide sequences without SEQ ID NO identifiers (e.g., paragraphs 0046-0047, references to peptides 1 and 7 in paragraphs 150-151, and others). The examiner has made an effort to identify these informalities. However, Applicant must carefully review the specification to identify and indicate where these informalities are to be found. Appropriate corrections are required to insert each SEQ ID NO to reflect specific peptide sequences. Applicant is reminded that no new matter may be introduced to the disclosure.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 1-2, 6 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Although the claims recite the limitation of selecting a target within the JNK pathway, the JNK pathway is intrinsically associated with many other pathways and the targets of these other pathways are not directly associated with the JNK pathway, *e.g.,* See page 448 of Ding and Yin (*J Cell Mol Med*, 2004, Vol 8 No. 4, pages 445-454), and it is unclear whether these targets are considered to be "within the JNK pathway. One of ordinary skill in the art would not be reasonably apprised of the scope of the invention as claimed. As such, the metes and bounds of the claimed invention cannot be determined.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

1. Claims 1-2, 6 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the ENABLEMENT requirement. The specification, while enabling for an *in vitro* method of modulating JNK pathway leading to programmed cell death comprising selecting a target within the JNK pathway leading to programmed cell death and interfering with said target by an agent, does not reasonably provide enablement for an *in vivo* method for modulating JNK pathway leading to programmed cell death comprising selecting a target and interfering with said target by an agent – as contemplated in the specification and inferred by the claims – for the treatment of cancer.

According to *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1998), the claimed invention should be enabled so that any person skilled in the art can make and use the invention without undue experimentation. See also United States v. Telectronics, Inc., 857 F.2d 778, 785, 8 USPQ2d 1217, 1223 (Fed. Cir. 1988) ("The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosures in the patent coupled with information known in the art without undue experimentation.") See also MPEP § 2164.01(a) and § 2164.04. Factors to consider in determining whether undue experimentation is required are summarized in *Ex parte Forman*, 230 USPQ 546 (BPAI 1986). The factors include the nature of the invention, the breadth of the claims, the state of the prior art, the relative skilled of those in the art, the amount of direction or guidance disclosed in the specification, the presence or absence of working examples, the predictability or unpredictability of the art, and the quantity of experimentation which would be required in order to practice the invention as claimed.

The claims are drawn to a method for modulating pathways leading to programmed cell death comprising selecting a target within the JNK pathway and interfering with said target by an agent that either upregulates or downregulates the JNK pathway (Claim 1), wherein obtaining an agent that is sufficient to block the suppression of JNK activation by Gadd45 proteins and contacting the cell with said agent to increase the percent of cells that undergo programmed cell death (Claim 2), wherein the agent is a cell-permeable peptide that competes with Gadd45β protein for the binding site of JNKK2. It is noted that the claims are drawn to both

in vivo and *in vitro* modulations wherein the *in vivo* modulations are drawn to a variety of diseases, including cancer.

The specification teaches that NF-kB plays a role in oncogenesis and that direct evidence from both *in vivo* and *in vitro* models suggests that its control of apoptosis is important for cancer development (para 00013). The specification teaches that JNK1/2/3 have a role in apoptosis (para 00015). The specification hypothesizes that inhibition of JNK ***might*** represent a mechanism by which NF-KB promotes oncogenesis and cancer chemoresistance (para (00017). In addition the specification teaches that Gadd45 has been linked to apoptosis in some systems. However it is not clear that this is a physiologic activity (para 00018). Although the specification further teaches that Gadd45 proteins have been proposed to be initiators of JNK, other reports have concluded that expression of these proteins does not induce JNK in various cell lines and the endogenous products make no contribution to the activation of JNK by stress (para bridging pgs 7 and 8). The specification further teaches that Gadd45B binds to and inhibits JNKK2, thereby downregulating the JNK pathway in vitro (para 00072). The specification hypothesizes that "potentially any agent capable of inhibiting Gadd45B either by interfering with the function of Gadd45 protein, or with the expression of the protein in cells" might be useful for treating cancer (000215). Finally, the specification states that NF-kB inhibitors are used in combination with standard anti-cancer agents to treat cancer patients yet they achieve only partial inhibition of NF-kB. The specification suggests that a better approach ***might be*** to employ agents that block, rather than NF-kB, its downstream anti-apoptotic effects in cancer cells (para 00020), apparently suggesting that inhibition of the proposed downstream effector, JNK would be useful in the treatment of cancer. The specification discloses that despite intense investigation, these effectors remain unknown (paragraph 0020). The specification teaches that since Gadd45β is able to bind to and inhibit JNKK2 activity *in vitro*, Gadd45β **likely blocks** this kinase directly, either by inducing conformational changes or steric hindrances that impede kinase activity (paragraph 0072). The specification provides a general method of screening for agents that prevent the ability of Gadd45β to block apoptosis in TNFα-sensitive and TNFα-resistant NF-kB-competent cell lines (paragraph 200+). Finally, the specification also provides general methods of measuring cytotoxicity (paragraph 227), apoptosis of BT-20 and MDA-MD-231 cells (paragraph 231), mobility shift on WEHI-231 cells

(paragraph 230), co-immunoprecipitation with 293 cell lysates (paragraph 232) and kinase activity of Gadd45β protein on HEK-293 cells.

One cannot extrapolate the teaching of the specification to the enablement of the claims because neither the art nor the specification teaches a nexus between *in vitro* downregulating JNK pathway in culture cells and the *in vivo* efficacy of treating a variety of diseases. It is well known in the art that cultured cells, over a period time, lose phenotypic characteristics associated with their normal counterpart cell type. Freshney (Culture of Animal Cells, A Manual of Basic Technique, Alan R. Liss, Inc., 1983, New York, p4) teaches that the art recognized many differences between cultured cells and their *in vivo* counterparts. These differences stem from the dissociation of cells from a three-dimensional geometry and their propagation on a two-dimensional substrate. Specific cell interactions characteristic of histology of the tissue are lost. The culture environment lacks the input of the nervous and endocrine systems involved in homeostatic regulation *in vivo*. Without this control, cellular metabolism may be more constant *in vitro* but may not be truly representative of the tissue from which the cells were derived. This has often led to tissue culture being regarded in a rather skeptical light (p. 4, see Major Differences *In Vitro*). Dermer (*BioTechnology*, 1994, 12:320) teaches that, a petri dish cancer is a poor representation of malignancy, with characteristics profoundly different from the human disease. Further, Dermer teaches that when a normal or malignant body cell adapts to immortal life in culture, it takes an evolutionary-type step that enables the new line to thrive in its artificial environment. This step transforms a cell from one that is stable and differentiated to one that is unstable, yet normal or malignant cells *in vivo* do not mimic the *in vitro* transformation. The reference states that evidence of the contradictions between life on the bottom of a lab dish and in the body has been in the scientific literature for more than 30 years. Clearly it is well known in the art that cells in culture exhibit characteristics different from those *in vivo* and cannot duplicate the complex conditions of *in vivo* environment involved in host-tumor and cell-cell interactions.

Although the specification teaches that overexpression of Gadd45 has been linked to apoptosis in some systems, there is no information provided concerning what these systems might be and no information had been provided drawn to the association of Gadd45β and apoptosis. Thus, it is assumed, for examination purposes, that the systems disclosed are cell culture systems. If it were to be determined that Gadd45β overexpression is associated with

apoptosis, it would still not e clear whether Gadd45β overexpression is an artifact of the cell culture systems or whether this can be in any way related to the *in vivo* cells from which the cell lines were derived, in view of the art recognized problems with artifacts associated with cell culture. For example, Drexler et al (Leukemia and Lymphoma, 1993, 9:1-25) specifically teach, in the study of Hodgkin and Reed-Sternberg cancer cells in culture, that the acquisition or loss of certain properties during adaptation to culture systems cannot be excluded. This is exemplified by the teachings of Zellner et al (*Clin. Can. Res.*, 1998, 4:1797-1802) who specifically teach that products are overexpressed in glioblastoma (GBM)-derived cell lines which are not overexpressed *in vivo*. Drexler et al further teach that only a few cell lines containing cells that resemble the *in vivo* cancer cells have been established and, even for the bona fide cancer cell lines, it is difficult to prove that the immortalized cells originated from a specific cancer cell (see attached abstract). Further, Embleton et al (*Immunol Ser*, 1984, 23:181-207) specifically teaches that, in procedures for the diagnosis of osteogenic sarcoma, caution must be used when interpreting results obtained with monoclonal antibodies that had been raised to cultured cell lines. Embleton *et al.* also specifically teach that cultured tumor cells may not be antigenically typical of the tumor cell population from which they were derived and it is well established that new artifactual antigens can occur as a result of culture (see attached abstract). Finally, Hsu (in Tissue Culture Methods and Applications, Kruse and Patterson, Eds, 1973, Academic Press, NY, see abstract, p.764) specifically teaches that it is well known that cell cultures *in vitro* frequently change their chromosomal constitutions (see abstract). It is clear that, based on the state of the art and in the absence of experimental evidence, no one skilled in the art would accept the assertion that the invention would function as inferred or contemplated in the *in vivo* environment.

As drawn to the inferred and contemplated treatment of diseases (e.g., cancer), one cannot extrapolate the teaching of the specification to the enablement of the claims because it is well known in the art that anticancer drug discovery for cancer therapy is highly unpredictable and Applicant has claimed an unspecified agent to target a broad number of targets to achieve an objective of modulating the JNK pathway. Gura (*Science*, 1997, 278:1041-1042) teaches that researchers face the problem of sifting through potential anticancer agents to find ones promising enough to make human clinical trials worthwhile. Gura also teaches that since formal screening began in 1955, many thousands of drugs have shown activity in either cell or animal models but that only 39 have actually been shown to be useful for chemotherapy (p. 1041, see

first and second para). As drawn to the unpredictability of the cancer therapy arts, the refractory nature of cancer to drugs is well known in the art. Jain (*Sci. Am.,* 1994, 271:58-65) teaches that tumors resist penetration by drugs (p.58, col 1) and that scientists need to put expanded effort into uncovering the reasons why therapeutic agents that show encouraging promise in the laboratory often turn out to be ineffective in the treatment of common solid tumors (p. 65, col 3). Curti (*Crit. Rev. in Oncology/Hematology*, 1993, 14:29-39) teaches that solid tumors resist destruction by chemotherapy agents and that although strategies to overcome defense mechanisms of neoplastic cells have been developed and tested in a number of patients, success has been limited and further teaches that it is certainly possible that cancer cells possess many as yet undefined additional molecular mechanisms to defeat chemotherapy treatment strategies and if this is true, designing effective chemotherapeutic regimens for solid tumors may prove a daunting task (para bridging pages 29-30) and concludes that knowledge about the physical barriers to drug delivery in tumors is a work in progress (p. 36, col 2).

Finally, an agent must accomplish several tasks to be effective toward any of the listed targets *in vivo*. It must be delivered into the circulation that supplies the tumor and interact at the proper site of action and must do so at a sufficient concentration and for a sufficient period of time. In addition, the target cell must not have an alternate means of survival despite action at the proper site for the agent. *In vitro* assays cannot duplicate the complex conditions of *in vivo* therapy. In the assays, the agent is in contact with cells during the entire exposure period. This is not the case *in vivo*, where exposure at the target site may be delayed or inadequate. In addition, variables such as biological stability, half-life or clearance from the blood are important parameters in achieving successful therapy. The claimed agent may be inactivated *in vivo* before producing a sufficient effect, for example, by proteolytic degradation, immunological activation or due to an inherently short half life of the protein and *in vitro* tests would not sufficiently duplicate the conditions which occur *in vivo*. In addition, the claimed agent may not otherwise reach the target because of its inability to penetrate tissues or cells where its activity is to be exerted, may be absorbed by cells and tissues where the claimed agent has no effect, circulation into the target area may be insufficient to carry the claimed agent and a large enough local concentration may not be established. For the above reasons, it appears that undue experimentation would be required to practice the claimed inventions with a reasonable expectation of success. Because of the known unpredictability of the art, in the absence of experimental evidence, no one skilled in the art would accept the assertion that any unspecified

agent, such as any peptide, would target any of the listed "targets" and function as claimed, based on an *in vitro* finding that Gadd45β binds to JNKK2.

It is noted that MPEP 2164.03 teaches that "the amount of guidance or direction needed to enable the invention is inversely related to the amount of knowledge in the state of the art as well as the predictability of the art. In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970). The amount of guidance or direction refers to that information in the application, as originally filed, that teaches exactly how to make or use the invention. The more that is known in the prior art about the nature of the invention, how to make, and how to use the invention, and the more predictable the art is, the less information needs to explicitly stated in the specification. In contrast, if little is known in the prior art about the nature of the invention and the art is unpredictable, the specification would need more detail as how to make and use the invention in order to be enabling."

It is noted that Applicant refers to in vitro assays as being drawn to "in vivo" studies (see paragraph 00067, 00070). This reference does not enable the claims because the assays are, in fact, done in vitro cell cultures. Given the unpredictability of identification of any agent, the lack of adequate disclosure in the specification, and in view of the complex nature of the claimed invention, and little is known in the art about the claimed invention, one of skill in the art would be forced into undue experimentation to practice the claimed invention.

2. Claims 1-2, 6 are rejected under 35 USC 112, first paragraph, as lacking an adequate WRITTEN DESCRIPTION in the specification. The claims contain subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are drawn to a method for modulating pathways leading to programmed cell death comprising selecting a target within the JNK pathway and interfering with said target by

an agent that either upregulates or downregulates the JNK pathway (Claim 1). The claim is also drawn to a method for modulating pathways leading to programmed cell death, said method comprising obtaining an agent that is sufficient to block the suppression of JNK activation by Gad45β protein; and contacting the cell with said agent to increase the percent of cell that undergo programmed cell death (Claim 2), wherein the agent is a cell-permeable peptide that competes with Gadd45β protein for the binding site of JNKK2 (Claim 6).

The claims are inclusive of using agents that include peptides, peptide mimetics, peptide-like molecules, mutant proteins, cDNAs, antisense oligonucleotides or constructs, lipids, carbohydrates, and synthetic or natural chemical compounds (paragraph 0031). The claims are also inclusive of any agent capable of inhibiting Gadd45β either by interfering with the function of Gadd45β protein, or with the expression of the protein in cells, which includes naturally-occurring or synthetic chemical compounds, anti-sense constructs or oligonucleotides, Gadd45β mutant proteins, mutant or wild-type forms of proteins that interfere with Gadd45β expression or function, anti-Gadd45β antibodies, cDNAs that encode any of the above mentioned proteins, ribozymes, synthetic peptides and the like (paragraph 0215). The agents above are identified as nonlimiting examples of agents that modulate the JNK pathway (e.g., paragraph 0031, 215), which means that other agents not mentioned in the specification are also contemplated by the invention.

Although drawn to the DNA arts, the finding in *University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997) and *Enzo Biochem, Inc. V. Gen-Probe Inc.* are relevant to the instant claims. The Federal Circuit addressed the application of the written description requirement to DNA-related inventions in *University of California v. Eli Lilly and Co.*, 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997). The court stated that "[a] written description of an invention involving a chemical genus, like a description of a chemical species, 'requires a precise definition, such as by structure, formula, [or] chemical name,' of the claimed subject matter sufficient to distinguish it from other materials." *Id.* At 1567, 43 USPQ2d at 1405. The court also stated that

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA" without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or

> recognize the identity of the members of the genus. A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is.

Id. at 1568, 43 USPQ2d at 1406. The court concluded that "naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material." Id.

Finally, the court addressed the manner by which a genus of cDNAs might be described. "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNAs, defined by nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus." *Id.*

The Federal Circuit has recently clarified that a DNA molecule can be adequately described without disclosing its complete structure. See *Enzo Biochem, Inc. V. Gen-Probe Inc.*, 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002). The *Enzo* court adopted the standard that "the written description requirement can be met by 'show[ing] that an invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics....i.e., complete or partial structure, other physical and/or chemical properties, functional characteristics when coupled with a known or disclosed correlation between function and structure, or some combination of such characteristics." Id. at 1324, 63 USPQ2d at 1613 (emphasis omitted, bracketed material in original).

The inventions at issue in *Lilly* and *Enzo* were DNA constructs *per se* and the holdings of those cases are applicable to the claims at issue here. A disclosure that does not adequately describe a product itself logically cannot adequately describe a method of using that product.

The instant specification may provide an adequate written description of the agents that upregulate or down regulate, per *Lilly* by structurally describing a representative number of agents that function as claimed or by describing structural features common to the members of the genus, which features constitute a substantial portion of the genus. Alternatively, per *Enzo*, the specification can show that the claimed invention is complete by disclosure of sufficiently detailed, relevant identifying characteristics, functional characteristics when coupled with a

known or disclosed correlation between function and structure, or some combination of such characteristics.

In the instant case, the specification does not adequately describe the genus of agents that either upregulates or downregulates the JNK pathway in a manner that satisfies either the *Lilly* or *Enzo* standards. There are no known structural or chemical features common to all members of the genus of agents as claimed. Out of the entire genus of agents, no particular agent is described. Claim 6 recites a cell-permeable peptide that competes with Gadd45β, however, no such peptide is identified in the specification. The only peptide that is identified in the specification that is cell-permeable is the HIV-TAT, which is well-known in the art to be cell-permeable and other peptides can link and be transported across the cell membrane (e.g., See Bonny *et al.* (*Diabetes*, January 2001, Vol 50, pages 77-82) and also well known to activate JNK pathway (e.g., see Kumar et al., *J. Immunol.* 1998, 161:776-781). However, it is uncertain whether HIV-TAT competes with Gadd45β for the binding site of JNKK2, and the specification fails to address this issue. Thus, the specification does not provide an adequate written description of the claimed genus of agents as set forth in *Lilly*. In addition, there is no functional characteristic common to the broad genus of agents; and thus, the claimed genus of agents does not meet the standard set forth in *Enzo*. In conclusion, the specification does not provide an adequate written description of the genus of agents that upregulate or downregulate that is required to practice the claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 1 is rejected under 35 U.S.C. 102(e) as being anticipated by Reinhard et al. (US Patent No: 6,492,112, filed December 1998).

Claim 1 is drawn to a method for modulating pathways leading to programmed cell death comprising selecting a target within the JNK pathway and interfering with said target by an agent that either upregulates or downregulates the JNK pathway.

Reinhard *et al.* teach a method of modulating a pathway leading to apoptosis by contacting a cell with a reagent which binds to the MKK7 (i.e., JNKK2) gene or expression product (column 2, lines 64-67), which is capable of interfering with, that is, phosphorylating a JNK substrate (column 8, lines 54-57) thereby preventing apoptosis (column 2, last paragraph). Reinhard *et al.* teach that peptides which can modulate signal transduction through a JNK pathway can be used to upregulate or downregulate the JNK pathway (column 19, lines 46-49), thereby increasing or decreasing the percentage of cells that undergo programmed cell death.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b). Effective January 1, 1994, a registered attorney or agent of

record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-2, 6 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over Claims 1-2, 6 of U.S. Application SN 10/263330 (Publication No: 20030077262, claims amended since the publication). This is a provisional double patenting rejection since the conflicting claims have not in fact been patented. Although the claims are not identical, they are not patentably distinct from each other because of the following:

> Claim 1 is drawn to a method for modulating pathways leading to programmed cell death, said method comprising selecting a target within the JNK pathway and interfering with said target by an agent that either upregulates or down regulates the JNK pathway. Claim 2 further limits Claim 1 said method comprising obtaining an agent that is sufficient to block the suppression of JNK activation by Gadd45 proteins and contacting the cell with said agent to increase the percent of cells that undergo programmed cell death. Claim 6 further limits Claim 2 wherein the agent is a cell-permeable peptide that competes with the Gadd45β protein for the binding site of JNKK2.
>
> Claim 1, last amended on July 15, 2005, is drawn to a method for modulating a JNK pathway leading to programmed cell death, said method comprising selecting a target wherein the target is Gadd45β or JNKK2 and interfering with a Gadd45β-JNKK2 interaction by an agent that either upregulates or downregulates the JNK pathway. Amended Claim 2 further limits Claim 1 wherein suppression of JNKK2 activation by a Gadd45β protein and increases the percent of cells that undergo programmed cell death. Amended Claim 6 further limits Claim 2 wherein the agent is a cell-permeable peptide that effectively competes with the binding site of Gadd45β.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the claims of the instant application, drawn to a method of modulating pathways leading to programmed cell death, have overlapping scope with the claims of pending Application SN 10/263330, drawn to a method for modulating a JNK pathway leading to programmed cell death wherein the target is Gadd45β or JNKK2.

Conclusion

No claim is allowed.

Contact Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Audrey S. Pham whose telephone number is (571) 272-3323. The examiner can normally be reached during the hours of 8:30 AM - 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew, can be reached during business hours at the telephone number: (571) 272-0787. The fax number for the organization, where this application or proceeding is assigned, is (571) 273-8300.

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